REMARKS

1. Claims 1, 3 5-7 and 9 were rejected by the Examiner under 35 USC §103(a) as being unpatentable over Minick et al. (J. Chrom. 461: 177-191 (1989)) and Abraham et al. The Examiner stated that it would have been obvious to one of ordinary skill in the art to chromatograph a sample in the system of Minick et al. and calculate log P from the correlations of Minick et al. in order to determine log P from and HPLC correlation as taught by Abraham. Applicants respectfully traverse this rejection.

The Examiner acknowledges that Minick et al. fails to teach that log D is determined from the equation for other samples or that the C18 column has "low silanol activity".

Applicants submit that a prima facie obviousness rejection has not been established based on the teaching of the Minick et al. paper and Abraham et al. paper for the following reasons. First, at page 178, second and third paragraphs, Minick et al. teaches that it is using, in this paper, the method recently published by Minick et al. (J.Med.Chem. (1988) 31, pp. 1923-1933) which was cited against the present application in the Office Action of September 29, 2003, and overcome in Applicants' response of January 29, 2004, as indicated in the present Office Action (mailed May 18, 2004) at page 4, paragraph 13. As Applicants stated in Amendment A dated 1/29/04, "while Minick et al. does disclose the use of a C18 column, the authors recommend using a C8 column as supported by their data. Note page 1928, column 1, paragraph 2 where it is stated '...C8 is the stationary phase of choice for modeling $\log P_{o/w}$.'" Moreover, at page 179, second full paragraph, Minick et al. teach using "5–µm octyl-modified silicas", which corresponds to a C-8 column. Thus one skilled in the art would not have been led to modify the C18 column as argued in the rejection. See in re Gurley, 31 USPQ2d 1130, 132 (Fed. Cir. 1994).

Second, Minick et al. (J. Chrom. 461:177-191 (1989)) teaches determination of log $P_{o/w}$ but not log D_{oct}. Abraham teaches determination of log P_{oct} as well. Thus, Minick et al. and Abraham et al. do not teach nor suggest the determination of log $D_{oct.}$ In contrast, the Applicants teach determination of log D_{oct} Log D_{oct} and log $P_{o/w}$ are different targets. Log $D_{oct,}$, the distribution coefficient, is broader than log $P_{o/w,}$ the partition coefficient. The present specification points out the difference: "At physiological pH many basic or acidic drugs are ionized, and the partition coefficient is indeed a distribution coefficient, D, which is generally taken to be the distribution

between an aqueous buffer at pH 7.4 and n-octanol, and it is indicated by the notation D_{oct}.." (specification page 1, lines 15-18.) Log $P_{o/w}$ is limited in scope, and deals only with neutral compounds. Log D_{oct} will look at ionized compounds as well as neutral compounds at pH 7.4, which is a physiologically relevant pH, and is relevant to the present application, which is directed at characterizing drugs. By definition, consideration of drugs at physiological pH is appropriate, as this is the condition under which they are used, and their lipophilicity as determined by the present method is of paramount importance in ADME properties. (see specification, page 1, lines 9-11). For these reasons, the combination of Minick et al. and Abraham do not make obvious the determination of log D_{oct}, as taught by Applicants.

Applicants, therefore, respectfully request the Examiner to reconsider the Office Action and withdraw the rejection of the claims 1, 3, 5-7 and 9 under 35 USC §103(a).

2. Claims 1-4 and 6-8 were rejected under 35 §102(a) over Lombardo et al. which Examiner says teaches correlating log P using and ABZ amide column and the claimed buffer conditions resulting in correlations with constant ranges which overlap the constant ranges of Eq. 1. Moreover, Examiner states that log P is the same as log D at pH values where the compounds are neutral. Applicants respectfully traverse this rejection.

Applicants submit that a prima facie anticipation rejection has not been established based on the teachings of the Lombardo et al. paper for the following reasons. Lombardo et al. is more similar to Minick et al.as the paper is determining log P_{oct}, rather than log D_{oct}. Log D_{oct} and log $P_{o/w}$ are different targets. Log D_{oct} is broader than log $P_{o/w}$. Log $P_{o/w}$ is limited in scope, and deals only with neutral compounds. Log D_{oct} will look at ionized compounds as well as neutral compounds at pH 7.4, which is a physiologically relevant pH, and is relevant to the present application, which is directed at characterizing drugs, which are used in a physiological system. Thus, the present application is not anticipated by Lombardo et al.

Applicants, therefore, respectfully request the Examiner to reconsider the Office Action and withdraw the rejection of the claims 1-4 and 6-8 under 35 USC § 102(a).

3. In view of the above remarks and amendments filed herewith, the Application and all of the claims are in condition for allowance and such favorable action is respectfully solicited. The Examiner is respectfully urged to contact the undersigned attorney for purposes of favorable advancing the prosecution of this Application.

Respectfully submitted,

Date: 10/18/2004

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